REMICADE® (infliximab) Clinical Medical Value Summary

REMICADE® has been used to treat more than 843,000 patients worldwide for immune mediated inflammatory disorders and is indicated for the treatment of patients with rheumatoid arthritis, ulcerative colitis, crohn’s disease, ankylosing spondylitis (as), psoriatic arthritis, and, most recently, psoriasis—more than any other anti-TNF-alpha therapy.¹ The safety profile of REMICADE has been evaluated in clinical trials and post-marketing surveillance for over 14 years.¹ The benefit:risk balance for patients continues to be consistently and predictably positive.

Mechanism of Action:

- REMICADE is a chimeric monoclonal antibody specific to TNF-α.¹,³ TNF-α plays a critical role in the development of chronic immune mediated inflammatory disease.³
- REMICADE prevents biological activity of TNF-α by neutralizing soluble TNF-α and causing dissociation of receptor bound TNF-α.² REMICADE has a greater binding strength for TNF-α than any other currently available anti-TNF agent.⁴-⁹

Clinical Differentiating Features of REMICADE

REMICADE is an appropriate treatment option for patients with moderate to severe levels of immune mediated inflammatory disease (I.M.I.D.) and who exhibit significant burden of illness.² REMICADE has demonstrated rapidity of onset of action, high rates of remission of symptoms, and significant duration of response across a wide range of I.M.I.D.s. REMICADE may be titrated to achieve the most effective response based on patient weight and therefore may offer a cost-effective treatment option for appropriate patients.²

Gastrointestinal Disease

- REMICADE is the only anti-TNF approved for use in gastrointestinal disease, including adult and pediatric Crohn’s disease and ulcerative colitis.¹²
- REMICADE is the only anti-TNF agent demonstrated to induce mucosal healing and allow for steroid tapering.²
- REMICADE is the only anti-TNF that induces growth velocity in children with Crohn’s disease¹⁰.
- In addition to inducing and maintaining response and remission in Crohn’s disease AND ulcerative colitis, REMICADE:
  - Reduces hospitalizations
  - Reduces the need for surgery
  - Improves quality of life (QoL)
  - Improves productivity²,¹¹-¹⁷

Psoriasis (PsO)

- REMICADE induces 75 to 100 percent skin clearance in patients with severe psoriasis.²,¹⁸
- REMICADE effectively improves healing of nail psoriasis in up to 50% of patients, a clinical advantage that has not been reported for other anti-TNF agents. Nail psoriasis can be particularly painful, severely limiting daily and work-related activities.¹,²,⁸,⁹,¹⁸
- REMICADE improves productivity and QoL, with the greatest improvement in QoL in patients with complete skin clearance.¹⁹
- In individual pivotal clinical trials, 8 out of 10 patients responded to REMICADE and 5 out of 10 patients responded to etanercept.¹⁸,²⁰
Rheumatoid Arthritis (RA)

- Only REMICADE and adalimumab (antibody TNF-alpha blockers) have demonstrated that they prevent radiographic progression in early and established MTX failures. Etanercept has not demonstrated this.\(^{22-32}\)
- Independent verification of the prevention of radiographic damage exists in the literature for REMICADE and adalimumab. There are no independent reports for etanercept.\(^{33-36}\)
- REMICADE is the only TNF blocker proven to have radiographic benefit following a switch from another TNF blocker.\(^{37-41}\)
- REMICADE is the only TNF blocker shown to induce drug-free remission in RA.\(^{33}\)
- REMICADE inhibits progression of structural damage by retaining joint space and reducing the number of erosions. Etanercept reduces the number of erosions but does not inhibit joint space narrowing.\(^{21-26}\)

Psoriatic Arthritis (PsA)

- REMICADE reduces pain and fatigue, restores function, and significantly improves quality of life, with greatest improvement in patients with both a joint and skin response.\(^{1,42}\)
- REMICADE improves productivity and employment status, and decreases lost time from work.\(^{43}\)
- REMICADE is effective against and reduces the percentage of patients with Dactylitis and Enthesitis associated with Psoriatic Arthritis. Adalimumab and Etanercept have not demonstrated efficacy with dactylitis or enthesitis in the published literature.\(^{42,44,45}\)
- REMICADE induces higher PASI-75 scores (clearance of skin plaques) in Psoriatic Arthritis patients compared to etanercept.\(^{2,8,42,45}\)

Ankylosing Spondylitis (AS)

- REMICADE improves spinal mobility and function, QoL, and productivity in patients with ankylosing spondylitis.\(^{2,46}\)
- Only REMICADE has demonstrated efficacy in AS-associated comorbidities (ex. gut manifestations of AS and PsA).\(^{47,48}\)
- REMICADE is the only anti-TNF agent effective in treating Dactylitis and Enthesitis associated with AS. Adalimumab demonstrated efficacy in a small (n=40) phase II study in patients with enthesitis, however efficacy with dactylitis has not been demonstrated in the published literature. Etanercept have not demonstrated efficacy with dactylitis or enthesitis in the published literature.\(^{2,8,9,49}\)

Route of Administration

- Intravenous route of administration provides for enhanced monitoring by healthcare professionals and may improve patient compliance with scheduled treatment regimens.\(^{2,50}\)
- REMICADE is administered every eight weeks based on body weight, whereas etanercept is administered once or twice weekly by injection in a static non-weight based regimen.\(^{2,8}\)
- The less frequent but larger dose of infliximab results in higher peak serum concentrations compared with the more frequent, smaller doses of etanercept. This could in turn could result in higher infliximab concentrations in diseased tissues and therefore greater efficacy in those tissues; this might also explain the need for increased doses (beyond reference dose) of other anti-TNF’s to achieve desired outcomes.\(^{4,51}\)

References:

1. Data on file Centocor, Inc.